Effects of Gabapentin on Postoperative Pain after Laparoscopic Cholecystectomy

Manu Bhardwaj[1], Sourabh Kumar[2]

ABSTRACT

Introduction: Postoperative pain prevention and treatment continues to be a major challenge in postoperative care. Gabapentin has recently become a part of a wide array of postoperative multimodal analgesic regimens. Present study evaluated the efficacy of oral gabapentin in relief of acute post-operative pain in laparoscopic cholecystectomy and also compared the efficacy of oral Gabapentin with that of oral Tramadol.

Material and Methods: Sixty ASA I and II physical status patients of both sexes between 20-60 years of age scheduled for elective laparoscopic cholecystectomy were enrolled into this prospective, double blinded, randomized sequential allocation study. Any patient who was unwilling and uncooperative, ASA III and IV physical status, patients having body weight exceeding 20% of ideal body weight, known hypersensitive to any drug, drug or alcohol abuse, pregnant patient, uncontrolled concomitant medical diseases, history of chronic pain conditions, impaired kidney or liver function, laparoscopic cholecystectomy converted to open cholecystectomy, in whom some kind of analgesics were administered within 48 hrs of planned surgery were excluded from the study.

Result: Sixty patients (30 males) were enrolled in the study with mean ages of all three groups range from 37.40±9.18 to 41.70±6.84. However the mean age, weight and sex distribution among different groups were statistically insignificant (P>0.05). Mean heart rate in various groups at different intervals were insignificant (p>0.05) in the intra operative period. Among group I, II and III in the postoperative period, changes in mean heart rate was statistically significant (p<0.05). The changes in mean SBP and DBP were statistically insignificant (p>0.05) intraoperatively in the three groups.

Conclusion: Premedication with oral 300 mg gabapentin provides better pain relief in the postoperative period as compare to oral 100 mg tramadol and placebo group with minimal side effects.

Keywords: Gaba, Pain, Post-Cholecystectomy, Tramadol

INTRODUCTION

Postoperative pain prevention and treatment continues to be a major challenge in postoperative care. Opioids are commonly used for postoperative pain management but they have a significant side effect such as nausea, vomiting, constipation, drowsiness, allergic reactions and urinary retention leading to restriction of their use. Other method such as epidural analgesia is an invasive procedure but require extra effort and are associated with serious complications. Nonsteroidal antiinflammatory drugs (NSAIDs) are also used for postoperative analgesia, but may cause epigastric pain, gastric ulceration and bleeding, renal toxicity and fluid retention, allergic reactions and heart failure. A multimodal approach is proposed to manage postoperative pain adequately with minimum drug side-effects. Considering that surgical stimulation is associated with peripheral and central sensitization, anti-hyperalgesic drugs can treat postoperative pain by preventing central nervous system pain hypersensitivity. Gabapentin has recently become a part of a wide array of postoperative multimodal analgesic regimens.[1,2] Gabapentin, a drug used for neuropathic pain acts on peripheral sodium channels, voltage dependent calcium channels, and decreases glutaminergic transmission in the spinal cord.[3-5] It also inhibits central neuronal sensitization and hyperalgesia by acting on calcium channels located at postsynaptic and presynaptic junctions resulting in the inhibition of the calcium influx thereby decreasing excitatory amino acid neurotransmission.[6,7] By decreasing the central sensory input processing[8], gabapentin is considered to provide preemptive analgesia hence, decreasing the incidence of hyperalgesia and allodynia after surgery. The opioid consumption was found to be reduced in several pain states when gabapentin was co-administered clinically. On the other hand, gabapentin might also be helpful in reducing the dependence and tolerance of opioids. It seems that gabapentin is relatively a pretty safe drug in terms of its tolerable effective doses with minor unwanted or side effects clinically (somnolence, dizziness, nausea, and vomiting). It does not induce hepatic enzymes, therefore, justifying its evaluation in postoperative. There are few studies on effect of Gabapentin on acute post-operative pain control in laparoscopic cholecystectomy.[9,10] Aim of present study was to evaluate efficacy of oral Gabapentin in relief of acute post-operative pain in laparoscopic cholecystectomy and also compare the efficacy of oral Gabapentin with that of oral Tramadol.

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MATERIAL AND METHODS

This study was conducted in the Department of anesthesiology and intensive care unit of the hospital. Prior to commencing the study, approval was obtained from both the ethical and hospital research committee. Patients to this study were explained of the anaesthetic procedure and informed consent was taken. Sixty ASA I and II physical status patients of both sexes between 20-60 years of age scheduled for elective laparoscopic cholecystectomy were enrolled into this prospective, double blinded, randomized sequential allocation study. Any patient who was unwilling and uncooperative, ASA III and IV physical status, patients having body weight exceeding 20% of ideal body weight, known hypersensitive to any drug, drug or alcohol abuse, pregnant patient, uncontrolled concomitant medical diseases, history of chronic pain conditions, impaired kidney or liver function, laparoscopic cholecystectomy converted to open cholecystectomy, in whom some kind of analgesics were administered within 48 hrs of planned surgery were excluded from the study.

All patients were premedicated with oral alprazolam 0.5mg on the Evening before surgery and two hours prior to surgery with few sips of water. Patients were randomly assigned to three groups as follows-

- Group I: Receive oral 300 mg Gabapentin two hours before surgery
- Group II: Receive oral 100 mg Tramadol two hours before surgery
- Group III: Receive oral placebo two hours before surgery.

In the operation theatre, patient inquired for 8 hrs fasting period and was being asked to void the bladder. Intravenous access was established using an 18 gauge cannula. All patients were monitored using pulse oxymeter-continuous recording, ECG-Continuous recording, NIBP-every 2.5 min interval and EtCO2-continuous recording after intubation.

Anaesthesia was induced with propofol 1-2.5mg/kg until loss of verbal command. Fentanyl 2 mcg/kg, vecuronium bromide 100 mcg/kg and lidocaine 1.5 mg/kg 90 sec. before intubation. Anaesthesia was maintained with propofol infusion 100-200 mcg/kg/min and 70% nitrous oxide in oxygen and intermittent vecuronium and fentanyl repeated at half hour interval. After completion of surgery neuromuscular blockade was reversed with glycopyrrolate 10 mcg/kg and neostigmine 50 mcg/kg. Patients were extubated when adequate spontaneous ventilation was achieved.

All patients were monitored for the following parameters intraoperatively:

1. Heart rate and oxygen saturation at the baseline,at the time of intubation and every 10 min afterward till the end of surgery.

2. Continuous ECG monitoring till the end of surgery. Non-invasive arterial blood pressure was taken at the baseline then after every 2.5 mins till completion of surgery.Continuous EtCO2 monitoring from the time of intubation till extubation of the patients.

5. The duration of the surgery in all three groups were noted. Postoperatively patients were assessed for pain by subjective (Pain was assess on a rupee or paisa scale (1 rupee=100 paisa, meaning No pain (0), Mild pain (25), Moderate pain (50), Severe pain (75), Unbearable pain (100) and objective method (using a visual analogue scale (VAS)of 0-10 cm (with 0=no pain and l0 = severe pain)recommended by Scott and Huskinson at regular interval(every 2 hrs for the initial 12 hrs and then every 3 hrs for the next 12 hrs).

The different complications occurring in all three groups during intra-operative and post-operative period were noted for adverse effect which includes from 0-9 (where 0= No untoward adverse effect, 1=Hypotension, 2=Hypoxia, 3=Bradycardia, 4=Vomiting/Nausea, 5=Restlessness/ Agitation, 6=Sedation, 7=Vertigo/Ataxia, 8=Pruritus, 9=Surgical complication).

Finally the impression of the patient was asked after one day of surgery. Post-operative analgesia was assessed by using visual analogue scale. From these data, the maximum pain scores at different time intervals (0-6,6-12,12-18,and 18-24 hours) for each patient was considered for statistical analysis. 2mcg/kg fentanyl was administered intravenously as a rescue analgesic on the patient's demand. The total fentanyl rescue dose requirement in 24 hr by each patient was recorded. The observation in the various groups were compared statistically using student 't' test/chi-square test analyzed by SPSS software of windows XP professional.

RESULT

The patient's demographic data were recorded and they were monitored for heart rate, systolic and diastolic blood pressure, oxygen saturation, intra-operative and postoperative over 24 hrs. Ramsay Sedations Score(RAS),Visual Analoggue Score (VAS), and rescue fentanyl used were recorded over 24 hrs post operative period for comparison among the groups.

Demographic data

Sixty patients (30 males) were enrolled in the study with mean ages of all three groups range from 37.40±9.18 to 41.70±6.84. However the mean age among different groups were statistically insignificant (P>0.05) (Table 1). Similarly the mean weight of all the three groups were statistically insignificant (p>0.05). The distribution of male to female in all the three groups range from 40% to 60%, had no statistical significance(p>0.05) (Fig.1).

Heart rate

Table 2 showed the comparison of mean heart rate in various groups at different intervals which clearly showed that they were comparable in the intra operative period and statistically insignificant (p>0.05). Group I and group II were comparable in the postoperative period for the initial 10 hours after which the comparison was statistically significant (p<0.05). In group I and III the changes in mean heart rate was statistically significant (p<0.05) throughout the 24rs post operative period. Similarly the changes in mean heart

rate in group II and III was statistically significant ($p<0.05$) throughout the 24hr post operative period except at 6hr, 8hr, 18hr and 24hr post operative period.

Blood pressure

Table 3 showed the comparison of mean systolic blood pressure (SBP) of patients during intraoperative and 24hr postoperative period in the three groups. The changes were statistically insignificant ($p>0.05$) intraoperatively in the three groups except at 30 min intraoperative period in group I vs II and group I vs III. The changes in mean SBP were statistically not comparable in group I and III and group II and III, in postoperative 24hr period except at 6hr in group I vs III and 8hr in group II vs III and hence group comparison was statistically significant ($p<0.05$).

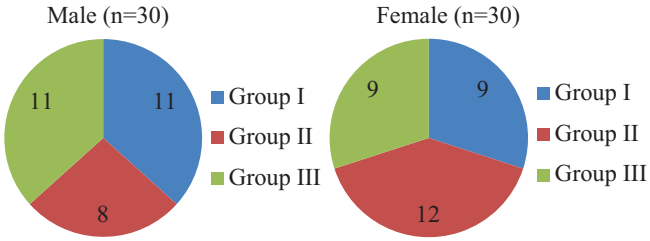

Figure-1: Sex distribution in various groups.

Table 4 showed the comparison of mean diastolic blood pressure (DBP) of patients during the intraoperative and over 24hr post operative period in three groups. The changes were statistically insignificant ($p>0.05$) intraoperatively in all three groups except at 40min intraoperative period.

The comparison of changes in mean DBP in group I vs III and in group II vs III over the 24hr postoperative period

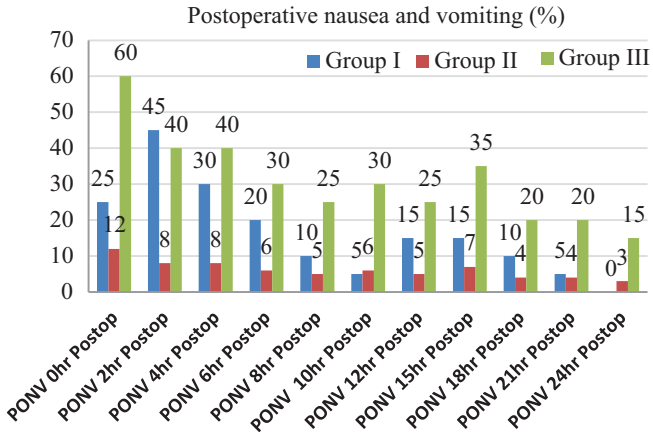

Figure-2: Postoperative nausea and vomiting in various groups at different interval

	GroupI Mean±SD (n=20)	Group II Mean±SD (n=20)	Group III Mean±SD (n=20)	Group I vs II	Group I vs III	Group II vs III
Age (years)	37.40±9.18	40.95±9.80	41.70±6.84	p0.245	p0.101	p0.781
Weight (kg)	52.70±3.08	52.0±6.17	53.36±4.28	p0.454	p0.339	p0.667
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-I: Distribution of cases according to age and weight in various groups

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
Baseline HR	72.80±5.04	72. 85±4.10	71.00±3.75	0.971	0.206	0.221
HR at induction	80.35±4.97	79.05±4.31	77.60±4.00	0.381	0.06	0.067
HR 10min	74.75±4.89	74.36±4.23	76.40±3.61	0.322	0.127	0.072
HR 20min	72.45±3.05	72.74±3.11	73.20±4.28	0.412	0.421	0.128
HR 30min	72.65±1.56	72.65±1.37	74.35±4.34	0.419	0.106	0.238
HR 40min	72.20±2.06	72.27±1.84	73.50±2.72	0.318	0.093	0.274
HR 50min	76.45±1.97	75.89±2.91	77.55±2.60	0.523	0.104	0.073
HR 0hr Postop	72.05±1.93	72.80±3.18	77.75±4.95	0.614	0.00*	0.007*
HR 2hr Postop	71.20±2.62	72.57±1.87	77.10±3.97	0.351	0.00*	0.008*
HR 4hr Postop	71.90±1.99	72.95±2.81	75.25±2.88	0.372	0.00*	0.037*
HR 6hr Postop	71.65±2.49	72.87±2.35	73.40±1.98	0.579	0.011*	0.621
HR 8hr Postop	73.90±3.55	73.15±2.51	75.15±2.51	0.446	0.029*	0.063
HR 10hr Postop	78.05±2.16	77.60±3.08	71.00±1.89	0.592	0.00*	0.00*
HR 12hr Postop	71.55±2.18	76.75±2.90	74.15±2.15	0.00*	0.001*	0.041*
HR 15hr Postop	71.60±3.57	76.75±3.85	74.65±2.39	0.00*	0.003*	0.048*
HR 18hr Postop	69.55±4.47	74.45±3.10	73.90±2.57	0.00*	0.00*	0.123
HR 21hr Postop	70.95±3.73	73.70±2.69	75.45±1.95	0.01*	0.00*	0.045*
HR 24hr Postop	72.25±1.77	74.35±3.43	74.45±3.60	0.02*	0.012*	0.328
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-2: Comparision of mean heart rate (per min) in various groups at different interval.

were statistically not comparable and hence statistically significant ($p<0.05$) except at 0 hr postoperative period and 12hr and 15hr postoperative period in group II vs III. The comparison in mean diastolic blood pressure changes in the postoperative period in group I vs II was comparable and hence statistically insignificant ($p>0.05$) except at 10hr 12hr and 15hr postoperative period.

Oxygen saturation

Table 5 showed the changes in mean oxygen saturation of patients in the three groups intraoperative as well as postoperative over a period of 24hr. The variation was around one to two percentage from baseline in all the groups except for few reading. Hence they were statistically insiginificant ($p>0.05$). Table 6 showed the comparison of the changes in mean oxygen saturation in the three groups over the

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
Baseline SBP	124.10±4.96	120.60±8.413	121.90±6.973	0.117	0.257	0.598
SBP at induction	128.20±3.83	127.20±7.381	128.40±5.826	0.594	0.899	0.572
SBP 10min	134.30±3.74	134.10±5.785	135.10±6.696	0.897	0.644	0.616
SBP 20min	130.40±4.52	127.80±5.578	125.40±3.500	0.114	0.781	0.111
SBP 30min	128.20±4.53	123.40±5.734	122.10±4.077	0.006*	0.00*	0.414
SBP 40min	125.60±4.07	124.10±5.210	123.20±5.634	0.315	0.13	0.603
SBP 50min	128.00±2.24	125.30±4.736	126.20±5.022	0.931	0.152	0.563
SBP 0hr Postop	124.10±4.96	125.10±4.789	129.60±3.470	0.521	0.00*	0.002*
SBP 2hr Postop	126.00±2.97	124.20±3.833	128.90±3.144	0.105	0.005*	0.00*
SBP 4hr Postop	124.20±4.04	124.70±2.536	127.80±2.505	0.642	0.002*	0.00*
SBP 6hr Postop	126.60±3.95	123.60±4.083	127.30±1.867	0.931	0.478	0.001*
SBP 8hr Postop	122.60±3.05	125.90±4.919	127.20±1.989	0.015*	0.00*	0.28
SBP 10hr Postop	124.40±3.58	125.20±4.275	129.10±2.864	0.525	0.00*	0.002*
SBP 12hr Postop	122.00±2.90	124.50±4.347	128.20±1.824	0.039*	0.00*	0.001*
SBP 15hr Postop	119.90±4.22	124.50±3.171	127.30±1.625	0.00*	0.00*	0.001*
SBP 18hr Postop	121.40±5.39	123.80±2.238	126.70±4.118	0.074	0.001*	0.009*
SBP 21hr Postop	122.40±3.01	122.90±2.553	125.00±3.340	0.575	0.014*	0.031*
SBP 24hr Postop	122.50±2.89	123.10±3.523	126.30±3.197	0.56	0.00*	0.005*
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-3: Mean systolic blood pressure (mmHg) in various groups at different interval

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
Baseline DBP	67.70±3.326	69.30±7.928	70.00±4.542	0.410	0.076	0.734
DBP at induction	73.20±3.397	74.90±7.799	75.20±1.881	0.377	0.314	0.868
DBP 10min	78.00±3.044	79.20±4.742	78.40±2.563	0.347	0.656	0.511
DBP 20min	74.40±3.409	75.80±7.730	75.10±2.713	0.463	0.477	0.704
DBP 30min	71.40±1.957	75.20±5.483	73.30±2.273	0.633	0.007*	0.160
DBP 40min	73.60±3.872	74.40±4.616	71.20±2.546	0.006*	0.026*	0.010*
DBP 50min	75.70±3.389	77.10±3.698	75.20±2.707	0.220	0.609	0.071
DBP 0hr Postop	73.80±2.331	74.90±2.789	74.10±2.292	0.184	0.684	0.328
DBP 2hr Postop	67.90±3.401	73.50±5.424	75.30±2.273	0.274	0.00*	0.015*
DBP 4hr Postop	71.10±1.651	69.30±7.928	76.30±3.326	0.326	0.00*	0.001*
DBP 6hr Postop	73.60±1.903	73.60±3.979	76.50±3.103	1.000	0.001*	0.014*
DBP 8hr Postop	72.60±3.560	73.40±3.440	77.00±3.811	0.474	0.001*	0.003*
DBP 10hr Postop	71.90±1.651	75.00±3.340	77.10±3.144	0.001*	0.00*	0.048*
DBP 12hr Postop	70.30±2.364	74.60±2.437	75.40±1.729	0.000*	0.00*	0.239
DBP 15hr Postop	69.60±2.479	76.00±5.731	75.90±3.144	0.000*	0.00*	0.946
DBP 18hr Postop	72.20±1.824	73.10±2.553	75.40±2.604	0.207	0.00*	0.008*
DBP 21hr Postop	73.20±2.093	72.40±6.108	75.70±1.750	0.583	0.00*	0.026
DBP 24hr Postop	70.70±3.262	69.80±6.802	74.60±2.162	0.597	0.00*	0.005
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-4: Mean diastolic blood pressure (mmHg) in various groups at different interval

same time interval which was comparable and statistically insignificant except for few readings.

Ramsay sedation score

Table 6 showed the changes in mean Ramsay sedations score of patients in the three groups postoperatively over a period of 24hrs. The variation of mean RSS was around one point in all the groups and hence comparable except at 4hr postoperative period. Comparison of changes in mean Ramsay sedations score in the three groups postoperatively over a period of 24hrs was observed. The variation was comparable and statistically insignficant (p>0.05) except at 4hr and 18hr postoperative period.

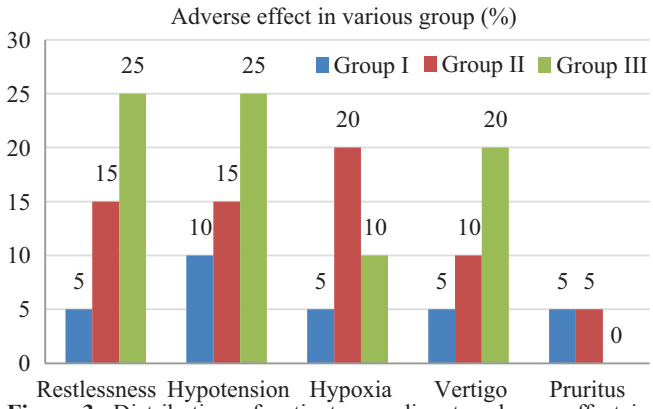

Figure-3: Distribution of patient according to adverse effect in various groups (in %)

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
Pre SPO2	97.90±0.55	98.20±0.89	97.95±0.68	0.21	0.8	0.32
SPO2 at induction	99.50±0.51	99.55±0.51	99.45±0.75	0.75	0.8	0.62
SPO2 10min	98.30±0.80	98.45±0.94	98.95±0.75	0.59	0.01*	0.07
SPO2 20min	99.15±0.93	98.40±0.88	98.50±1.19	0.01*	0.06	0.76
SPO2 30min	99.35±0.67	98.55±0.75	99.20±0.76	0.00*	0.51	0.01*
SPO2 40min	99.65±0.48	99.25±0.71	98.95±0.82	0.04*	0.00*	0.22
SPO2 50min	98.05±0.88	98.90±1.02	98.70±0.86	0.00*	0.02*	0.50
SPO2 0 hr Postop	98.80±0.83	98.60±1.04	99.05±0.88	0.50	0.36	0.15
SPO2 2hr Postop	99.15±1.04	98.90±0.85	98.85±1.13	0.41	0.38	0.87
SPO2 4hr Postop	99.30±0.92	99.00±0.97	99.30±0.73	0.32	1.0	0.27
SPO2 6hr Postop	98.50±0.68	98.75±0.78	98.70±0.73	0.29	0.37	0.83
SPO2 8hr Postop	98.35±0.81	98.60±0.68	99.05±0.88	0.29	0.01*	0.08
SPO2 10hr Postop	98.80±1.00	98.95±1.05	99.00±1.12	0.64	0.55	0.88
SPO2 12hr Postop	98.75±0.78	98.50±0.60	98.45±0.88	0.26	0.26	0.83
SPO2 15hr Postop	98.80±1.05	98.85±0.93	98.80±0.83	0.87	1.0	0.85
SPO2 18hr Postop	98.60±0.99	98.25±0.85	98.90±0.78	0.23	0.29	0.01*
SPO2 21hr Postop	98.80±0.95	98.90±0.85	98.55±0.94	0.72	0.41	0.22
SPO2 24hr Postop	99.00±0.97	99.40±0.75	99.10±0.85	0.15	0.73	0.24
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-5: Mean oxygen saturation % in various groups at different interval.

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
RSS 0hr Postop	2.95±0.605	3.40±0.754	3.10±0.788	0.044*	0.504	0.226
RSS 2hr Postop	2.55±0.510	2.75±0.716	3.05±1.146	0.316	0.083	0.327
RSS 4hr Postop	2.55±0.510	2.20±0.410	3.20±0.834	0.022*	0.005*	0.000*
RSS 6hr Postop	2.20±0.410	2.45±0.510	2.65±1.268	0.096	0.139	0.517
RSS 8hr Postop	2.15±0.366	2.55±0.510	2.25±0.550	0.007*	0.503	0.082
RSS 10hr Postop	2.30±0.470	2.35±0.470	2.70±0.733	0.744	0.047*	0.084
RSS 12hr Postop	2.45±0.510	2.55±0.510	2.35±0.671	0.539	0.599	0.295
RSS 15hr Postop	2.35±0.489	2.35±0.489	2.15±0.366	1	0.152	0.152
RSS 18hr Postop	2.15±0.366	2.50±0.513	2.50±0.513	0.018*	0.018*	1.000
RSS 21hr Postop	2.40±0.503	2.45±0.510	2.55±0.510	0.757	0.355	0.539
RSS 24hr Postop	2.30±0.470	2.45±0.510	2.55±0.510	0.34	0.115	0.539
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-6: Mean Ramsay sedation score in various groups at different interval

Visual analogue score (VAS)

The mean VAS was definitely higher in the group III as compared to that in group I and group II. Among three groups the mean VAS was lowest in group I. Table 7 showed the comparison of the mean VAS of Patients in the three groups postoperatively over a period of 24hr showing that the changes were not comparable among group I vs III and group II vs III and hence data were statistically significant ($p<0.05$). It was also found that the mean VAS among group I and II were comparable for the initial 6hrs postoperatively after which the data were not comparable signifying that the mean VAS was statistically significant after the initial 6hrs in the postoperative period among group I and II.

Fentanyl use

Table 8 showed that the comparison of the mean fentanyl use in patients in the three group over 24 hr postoperative period which clearly showed that the data were not comparable in group III as compared to group I and II and hence statistically significant ($p<0.05$). Similarly the comparison among the group I and II showed that the data was comparable and hence insignificant ($p>0.05$) in the initial 6hrs postoperative period.

Nausea and vomiting

Figure 2 showed that the incidence of post operative nausea and vomiting was higher at every time interval in group III than in the rest two groups. Among group I and II the incidence was higher in group II at every time interval except at 2hr 4hr 8hr and 15hr postoperative period

Adverse events

The incidence of complications in various groups is shown in figure 3. Restless/agitation occurred in one (5.00%) patient in group I as compared to three (15%) in group II and five (25%) in group III. Restlessness was relieved which injection of midazolam 1-2 mg intravenous. It was highly significant in group III ($p<0.05$). The incidence of hypotension was two (10.00%) in group I, three (15.00%) in group II and five 25.00% in group III. The incidence was highly significant in group III ($p<0.05$). it was manage by injecting mephentermine 5-10 mg intravenously. The incidence of hypoxia / respiratory depression was one (5.00%) in group I,

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
VAS 0hr Postop	0.25±0.444	0.45±0.510	1.50±0.946	0.194	0.000*	0.000*
VAS 2hr Postop	5.60±0.598	6.15±0.671	8.30±0.657	0.198	0.000*	0.000*
VAS 4hr Postop	4.15±0.745	4.00±0.858	6.45±1.146	0.559	0.000*	0.000*
VAS 6hr Postop	4.55±0.510	4.75±0.639	5.85±0.671	0.281	0.000*	0.000*
VAS 8hr Postop	1.95±0.759	4.10±0.912	6.25±1.164	0.000*	0.000*	0.000*
VAS 10hr Postop	2.95±0.605	4.70±0.979	5.20±0.894	0.000*	0.000*	0.100
VAS 12hr Postop	2.45±1.317	3.85±0.933	4.55±0.686	0.000*	0.000*	0.010*
VAS 15hr Postop	2.35±1.531	2.90±1.651	5.15±0.813	0.282	0.000*	0.000*
VAS 18hr Postop	1.75±0639	1.50±1.192	4.30±1.593	0.414	0.000*	0.000*
VAS 21hr Postop	0.65±0.489	1.40±0.883	3.40±0.503	0.002*	0.000*	0.000*
VAS 24hr Postop	1.60±0.503	0.80±0.696	2.00±0.795	0.000*	0.065	0.000*
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-7: Mean visual analogue score in various groups at different interval

Variables	Group I (n=20)	Group II (n=20)	Group III (n=20)	p value		
	Mean±SD	Mean±SD	Mean±SD	Group I vs Group II	Group I vs Group III	Group II vs Group III
Fenta 0hr Postop	0.00±0.00	0.00±0.00	0.00±0.00			
Fenta 2hr Postop	100.00±0.00	100.00±0.000	100.00±0.00			
Fenta 4hr Postop	35.00±48.936	15.00±36.635	100.00±0.00	0.152	0.00*	0.000*
Fenta 6hr Postop	55.00±51.042	65.00±48.936	100.00±0.000	0.531	0.00*	0.003*
Fenta 8hr Postop	0.00±0.00	45.00±51.042	100.00±0.00	0.000*	0.000*	0.000*
Fenta 10hr Postop	0.00±0.00	55.00±51.042	70.00±47.016	0.000*	0.00*	0.340
Fenta 12hr Postop	15.00±36.635	30.00±47.016	65.00±48.936	0.000*	0.001*	0.027*
Fenta 15hr Postop	20.00±41.039	30.00±47.016	75.00±44.426	0.000*	0.00*	0.004*
Fenta 18hr Postop	0.00±0.00	0.00±0.000	35.00±48.936		0.003*	0.003*
Fenta 21hr Postop	0.00±0.00	0.00±0.00	0.00±0.00			
Fenta 24hr Postop	0.00±0.00	0.00±0.00	0.00±0.00			
*P < 0.05 Demonstrate significant at 95% CI. SD: Standard deviation						

Table-8: Mean fentanyl used in various groups at different interval

four (20.00%) in group II and 2 (10.00%) in group III. It was statically significant in group II (P<0.05).

DISCUSSION

Pain, which is often inadequately treated, accompanies alrnost all surgical procedures and may persist long after tissue heals. In addition to immediate unpleasant and noxious experience,pain can imprint themselt on the nervous system, amplifying the response to subsequent noxious stimuli (hyperalgesia) and even causing typically painless experience to be painful (allodynia). Preemptive analgesia, involves the introduction of an analgesic regimen before the onset of noxious stimuli with the goal of preventing sensitization of the nervous system to subsequent stimuli that could amplify pain.[11] Gabapentin and Tramadol both have demonstrated analgesic effects in clinical trails as a preemptive analgesic and in acute postoperative pain management.[12] Gabapentin a GABA analogue is an antiepileptic drug also displays its antinociceptive activity in various animal pain models. Though the exact mechanism of action is not known, proposed mechanism (Cheng J K et al[13]) are its ability to increase the concentration of GABA in brain, Increase NMDA current at GABAergic interneurons, decrease in Glutamate level in brain, activate ATP sensitive K+channels, inhibit the voltage dependent Na^+ channels, increase in Ca^{++} current by binding to voltage dependent Ca++ channels.

The present study was conducted on Sixty ASA I and II physical status patients of either sex between 20-60 vears of age to evaluate and compare the preemptive effects of gabapentin and tramadol on postoperative pain and fentanyl requirement as rescue analaesic in patients scheduled for elective laparoscopic cholecystectomy. Patients were allocated randomly into three groups of twenty each as follows: Group I-Receive oral 300 mg Gabapentin 2 hours before surgery, Group II-Receive oral 100 mg Tramadol 2 hours before surgery, Group III-Receive oral Placebo 2 hours before surgery. In all groups, anaesthesia was induced with 1-2.5mg/kg propofol till loss of verbal command, fentanyl 2mcg/kg, vecuronium bromide 100 mcg/kg and lidocaine 1.5 mg/kg 90 sec. before intubation and maintained with propofol infusion 100-200 mcg/kg/min,70% N2O in Oxygen and intermittent vecuronium bromide and fentanyl at half hour interval. Patients were reversed after completion of surgery with glycopyrolate 10 mcg/kg and neostigmine 50 mcg/kg.

The patient's demographic data were recorded and monitored for haemodynamic parameters intraoperatively and postoperatively over 24 hours. Ramsay Sedation Score, Visual Analogue Score and rescue fentanyl used were recorded over 24 hours post-operative period for comparison among the groups. The mean age in group I(37.40±9.18),group II(40.95±9.80)and group III(41.70±6.84)and the mean weight in group I(52.70±3.08)group II (52.00±6.17) and group III (53.36±4.28)clearly showed that they were comparable among themselves and hence statistically insignificant(P>0.05). The sex distribution among the three groups range from 40%-60% and were comparable hence statistically insignificant (P>0.05).

The heart rate, systolic and diastolic blood pressure comparison among the three groups were statistically insignificant (P>0.05) during intraoperative period except for a few readings which can be attributed to the effect of pneumoperitoneum created for the surgery. Comparison of heart rate, systolic and diastolic blood pressure among group I vs III and group II vs III were significant in the postoperative period showing that the patients in group III were having pain and hence haemodynamically unstable. Comparing the same in group I vs II showed that the changes were significant after 10 hours postoperative period suggesting that the pain relief in gabapentin group was better and extend for the 24 hours postoperative period while tramadol was better in the initial 10 hours postoperative period.

In a study done by CK Pandey et al[14], he observed similar findings with regard to haemodynamic changes in the postoperative period. He observed that patients in gabapentin group had significantly lower pain scores at all time intervals in comparison to tramadol and placebo.Significantly less fentanyl was consumed in gabapentin group than in tramadol and placebo group.

Similarly SPO2 comparison in the three groups showed insignificant rhanges except tor a few readings which was attributed to the respiratory depression caused by tramadol. Similar finding was observed in his study.

Comparison of mean Ramsay sedation score showed insignificant changes over the 24 hours postoperative period in our study except for a few readings which was attributed to the sedation effect caused by midazolam given for the treatment of restlessness in the patients. Similar observation was seen in the study done by CK Pandey et al[14] and Seib R K. et al[15].

Comparison of mean visual analogue score in various groups oven the 24 hours postoperative period in the present study showed that mean VAS was statistically significant in group III as compared to group I and group II while comparing group I and II the data was statistically significant after 6 hours postoperative period. This shows that the gabapentin was definitely better in pain relief while tramadol was comparable to gabapentin only in initial 6 hours postoperative period.ck.[14]

In a study Fassoulaki A et al[16] observed the analgesic effect of gabapentin for breast cancer surgery. In his study it was found gabapentin reduce the postoperative analgesic requirement and pain scores upto fifth postoperative day.

Comparison of mean fentanyl used in patients in various group at different interval in the present study showed that the data was significant when group III was compared to group I and II while comparison of group I vs II showed that the data was significant in the postoperative period after 6 hours. This suggests that less fentanyl was used in gabapentin group than the rest two groups. Gabapentin and tramadol group were similar in the pain relief till 6 hours postoperative after which gabapaentin was found to be better.[14,15]

The incidence of Nausea and vomiting was higher in group II while lowest in group I in the present study but in the

study of CK Pandey et al[14] the incidence of nausea and vomiting was highest in the gabapentin group. The finding in our study can be attributed to the side effect of fentanyl which was used in higher amount in group III. In a different study by CK Pandey et al[17] it was observed that incidence of postoperative nausea and vomiting within 24 hours after laparoscopic cholecystectomy was significantly lower in gabapentin group(46/125) than in placebo group (75/125). There was a significant decrease in fentanyl consumption in gabapentin group as compared to placebo in his study.

The incidence of restlessness/agitation was highest in the placebo group in our study which can be attributed to the higher incidence of pain in that group. Similar finding was seen in CK Pandey et al[14] and Seib RK et al[15] study. Restlessness was relieved with injection Midazolam 1-2mg intravenous.

The incidence of hypotension was also highest in the placebo group which was managed by injection mephentermine 5-10 mg intravenously. Similarly the incidence of hypoxia/ respiratory depression was highest in tramadol group which was managed by supplementing with oxygen by ventimask. Ihe incidence of vertigo was two (10.00%) in the tramadol group, four (20.0%) in placebo group.CK Pandey et al[14] also observed the same finding that the incidence of vertigo was highest in placebo group.

CONCLUSION

In conclusion present study found that the patients taking gabapentin and tramadol respectively had better pain relief than the patients taking placebo and require less fentanyl as rescue analgesic. As far as complications were concerned the incidence of post operative nausea and vomiting was found to be less with gabapentin than in tramadol and placebo group. Patients in placebo group were having higher incidence of restessness and hypotention. The incidence of respiratory depression and hypoxia was higher with tramadol. Thus, we can summarise that premedication with oral 300 mg gabapentin provides better pain relief in the postoperative period as compare to oral 100 mg tramadol and placebo group with minimal side effects.

REFERENCES

1. Kehlet H, Dahl JB. Anaesthesia, surgery, and challenges in postoperative recovery. Lancet. 2003;362:1921–28.
2. Dahl JB, Mathiesen O, Kehlet H. An expert opinion on postoperative pain management, with special reference to new developments. Expert Opin Pharmacother. 2010;11:2459–2470.
3. Sills GJ. The mechanisms of action of gabapentin and pregabalin. Curr Opin Pharmacol. 2006;6:108–13.
4. Aksh TL. Calcium channels as therapeutic targets in neuropathic pain. J Pain. 2006;7:S13–S30.
5. Rosner H, Rubin L, Kestenbaum A. Gabapentin adjunctive therapy in neuropathic pain states. Clin J Pain 1996; 12:56–58.
6. Gottrup H, Juhl G, Kristensen AD. Chronic oral gabapentin reduces elements of central sensitization in human experimental hyperalgesia. Anesthesiology. 2004;101:1400–08.
7. Penprase B, Brunetto E, Dahmani E, Forthoffer JJ, Kapoor S. The efficacy of preemptive analgesia for postoperative pain control: a systematic review of the literature. AORN J. 2015;101:94–105.
8. Agarwal MM, Elsi Sy M. Gabapentenoids in pain management in urological chronic pelvic pain syndrome: gabapentin or pregabalin? Neurourol Urodyn 2017;36:2028-2033.
9. Eidy M, Fazel MR, Abdolrahimzadeh H, Moravveji AR, Kochaki E, Mohammadzadeh M. Effects of pregabalin and gabapentin on postoperative pain and opioid consumption after laparoscopic cholecystectomy. Korean J Anesthesiol. 2017;70:434–438.
10. Nakhli MS, Kahloul M, Jebali C, Frigui W, Naija W. Effects of Gabapentinoids Premedication on Shoulder Pain and Rehabilitation Quality after Laparoscopic Cholecystectomy: Pregabalin versus Gabapentin. Pain Res Manag. 2018;9:9834059.
11. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg. 1993;77:1048-56.
12. Gottschalk A, Smith DS, Jobes DR, Kennedy SK, Lally SE, Noble VE. Preemptive epidural analgesia and recovery from radical prostatectomy: a randomized controlled trial. JAMA. 1998;279:1076-82.
13. Cheng JK, Chiou LC. Mechanisms of the antinociceptive action of gabapentin. J Pharmacol Sci. 2006;100:471-86.
14. Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anaesth. 2004;51:358-63
15. Seib RK, Paul JE. Preoperative gabapentin for postoperative analgesia: a meta-analysis. Can J Anaesth. 2006;53:461-9.
16. Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q. The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. Anesth Analg. 2002;95:985-91.
17. Pandey CK, Priye S, Ambesh SP, Singh S, Singh U, Singh PK. Prophylactic gabapentin for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. J Postgrad Med. 2006;52:97-100.

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